

Attorney Docket No.: 13257.00044 (UMD-0084)
Inventors: Sciorra and Zimnoch
Serial No.: 09/869,741
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REMARKS

Claims 1-24 and 26-39 are pending in the instant application. Claims 1-24 and 26-39 have been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Withdrawn Rejections

Applicants acknowledge the withdrawal of the previous Office Action's rejections under 35 U.S.C. §103.

II. Rejections Under 35 U.S.C. §103

Claims 1-9, 12, 14, 16-20, 22-24, 26-29 and 37-39 have been newly rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (U.S. Patent No. 5,602,042) in view of Steindler et al. (U.S. Patent No. 6,638,763). It is suggested that Farber teaches a method and apparatus for magnetically separating biological particles from a mixture. It is suggested that Farber teaches many of the essential features of the claimed method with the exception of placing the suspension of sample and magnetic particles onto a substrate material, wherein the substrate material comprises a viscous solution; the substrate material is methylcellulose and the solution is between 1.7% and 2% methylcellulose. The Examiner suggests that Steindler et al. teach that methylcellulose is a viscous bioorganic solution which is used for cell separation, wherein by its viscous nature, methylcellulose limits contacts between cells and a substrate and allows clonal analysis. It is suggested that it would have been obvious to one of skill in the art to add methylcellulose as taught by Steindler et al. to the suspension of magnetic

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particles and target of Farber to separate cells and prevent cells from contacting the substrate or from aggregating with other cells in the solution. Since methylcellulose solution can form a gel at lower temperature, it can prevent diffusion of the magnetic component unless a magnetic force is applied according to the method of Farber. It is further suggested that it would have been obvious to use the methylcellulose at a range of 1.7% to 2.0% because discovering optimal ranges involves routine skill in the art.

Claims 32-36 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (U.S. Patent No. 5,602,042) in view of Steindler et al. The Examiner suggests that while Farber and Steindler et al. do not teach the frequency at which the magnetic field is activated or deactivated is from about 0.5 to 10 seconds per pulse or 2.0 seconds per pulse; and a magnetic field strength of about 1.5 to 2.0 or at least 3.0 Tesla, it would have been obvious to one of skill in the art to arrive at these specific pulse ranges and magnetic field strengths since discovering the optimum or workable ranges involves only routine skill in the art.

Claims 10, 11, 13, 15, 21, and 30 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (U.S. Patent No. 5,602,042) in view of Steindler et al. as applied to claims 1-9, 12, 14, 16-20, 22-24, 29, 37-39 above and further in view of Terstappen et al. (U.S. Patent No. 5,646,001). It is suggested that while Farber and Steindler et al. do not teach the elements of the rejected claims, Terstappen et al. disclose these elements.

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Claim 31 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Farber (U.S. Patent No. 5,602,042) in view of Steindler et al. as applied to claim 1, and further in view of Tseng-Law (U.S. Patent No. 6,017,719). It is suggested that while Farber and Steindler et al. fail to teach labeling non-target substances with a fluorescent marker, Tseng-Law et al. teaches positive and negative methods of cell selection from a cell suspension, wherein the positive cells are labeled with a fluorescent marker.

Applicants respectfully traverse these rejections.

MPEP §2143 clearly indicates that to establish a *prima facie* case of obviousness, three basic criteria first must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The cited prior art references fail to meet these three basic criteria.

The abstract of Farber teaches that the apparatus and method disclosed therein is for automated collection and transfer of particles from a liquid suspension to a glass slide for visual inspection. The abstract specifies that:

"[a] magnet is positioned adjacent to a solution which contains particles tagged with magnetic beads, for example cells, so that the magnetic particles flow toward the magnet and collect against a collection surface positioned between the particles and the magnet. A transfer mechanism applies a selected pressure to a second side of the collection surface for transferring collected cells to a viewing slide. The

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apparatus includes a device for dispersing the liquid suspension prior to the collection process and for collecting particles against the collection surface with a spatial distribution advantageous for visual examination."

While Farber teaches suspending magnetically tagged particles in a solution characterized as a liquid (see line 2 of the abstract) or fluid (see column 6, line 35), nowhere do Applicants find a teaching or suggestion to make modifications to the apparatus of Farber to employ a viscous solution that substantially prevents diffusion of a magnetic component unless a magnetic force is applied. In so far as Steindler et al. merely teach the use of methylcellulose for producing suspension cultures (see column 6, lines 7-26, and Example 6), this reference also fails to teach or suggest the use of a viscous solution for preventing diffusion of a magnetic component unless a magnetic force is applied.

For a *prima facie* case of obviousness to exist, there must be "some objective teaching in the prior art or ... knowledge generally available to one of ordinary skill in the art [that] would lead that individual to combine the relevant teachings of the references." *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). Because there is simply no objective teaching provided by either Farber or Steindler et al. to combine the teachings therein, it appears that the Examiner has relied upon an unsupported notion of what was generally available to one of ordinary skill in the art as motivation to combine the teachings of Farber and Steindler et al.

However, the presence or absence of a motivation to combine references is a question of fact, *In re Dembiczak*, 175 F.3d 994, 1000 (Fed. Cir. 1999), which is evaluated under the substantial

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evidence standard. *Gartside*, 203 F.3d at 1316. The Examiner's assumptions concerning motivation to modify the apparatus of Farber with the methylcellulose of Steindler et al. appears to rest on a generalized statement that "it would have been obvious to one of ordinary skill in the art to add methylcellulose as taught by Steindler to the suspension of magnetic particles and target of Farber to separate cells and to prevent cells from contacting the substrate (such as unbound magnetic particles, other magnetic particles in the solution, or the bottom of the container holding the suspension) or from aggregating with other cells in solution" without regard to the desirability of modifying the apparatus of Farber.

It is respectfully submitted that the Examiner's rationale for employing the methylcellulose of Steindler et al. to "prevent cells from contacting the substrate ... or from aggregating with other cells in solution" fails to take into consideration the fact that Farber specifically addresses this issue by employing "a device for dispersing the liquid suspension prior to the collection process." See abstract. Because the dispersion device of Farber provides shear forces to the fluid sample to disperse cells in the sample fluid (see column 8, lines 16-25), there would be no desirability and thus no motivation to modify the apparatus of Farber to employ the methylcellulose of Steindler et al.

Furthermore, while Steindler et al. teach that methylcellulose is a viscous bioorganic solution which limits contacts between cells and between cells and a substrate, this reference does not specifically teach that the methylcellulose prevents diffusion. Moreover, the Examiner has not provided any

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evidence of record to substantiate that the methylcellulose of Steindler et al. prevents diffusion.

Under MPEP §2144.03, it is never appropriate to rely solely on "common knowledge" in the art without evidentiary support in the record, as the principal evidence upon which a rejection was based. *Zurko*, 258 F.3d at 1385, 59 USPQ2d at 1697. *Cf. Kotzab*, 217 F.3d at 1371 ("[P]articular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."). The Examiner has not provided a factual record that establishes substantial evidence of a motivation to combine Farber with Steindler et al.

Thus, the statements made by the Examiner amount to no more than unsupported conclusory statements of generalized advantages and convenient assumptions about skilled artisans. However, such statements and assumptions are inadequate to support a finding of motivation, which is a factual question that cannot be resolved on "subjective belief and unknown authority." *Lee*, 277 F.3d at 1344. Therefore, Applicants respectfully submit that the Examiner has not met the first criterion for establishing a *prima facie* case of obvious under 35 U.S.C. 103(a).

Likewise, it is respectfully submitted that the cited prior art references fail to meet the third criterion for establishing a *prima facie* case of obvious, *i.e.*, the prior art reference (or references when combined) must teach or suggest all the claim limitations. In this regard, the instant method requires the steps of

placing the suspension onto a substrate material, wherein the substrate material comprises a viscous solution that substantially prevents diffusion of the

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magnetic component unless a magnetic force is applied and exposing the substrate material containing the suspension to a magnetic field of sufficient strength to cause the magnetic component to migrate across the substrate material.

While Farber teaches submerging a magnetic plate into a fluid sample so that magnetically tagged particles in the fluid sample flow toward the magnet and are collected on the surface of the plate (column 6, line 61, to column 7, line 47; and abstract) and Steindler et al. teach cells suspended in methylcellulose (see column 6, lines 7-26), neither Farber nor Steindler et al. teach or suggest placing a suspension onto a substrate composed of a viscous solution so that magnetic components in the suspension migrate across the substrate material.

MPEP §2143.03 states that all claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). In this regard, Applicants respectfully submit that the combined teachings of Farber and Steindler et al. fail to teach or suggest the all the limitations of the claims and therefore cannot be held to make the present invention obvious.

Because there is no teaching, suggestion or motivation to combine the teachings of the Farber and Steindler et al. and these references further fail to teach or suggest all claim limitations, a *prima facie* case of obviousness has not been established. In so far as the teachings of Terstappen et al. and Tseng-Law et al. fail to compensate for the deficiencies in the teachings of the primary and secondary references, it is

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respectfully submitted that the rejections of claims 1-24 and 26-39 under 35 U.S.C. 103(a) be withdrawn.

III. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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Date: November 10, 2006

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